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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/716,209	10/09/96	PRADIER	ST94014-US

EXAMINER: L

HM22/0211

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ART UNIT	PAPER NUMBER
1645	18

DATE MAILED: 02/11/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 8/24/98

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 27-29, 31-54 is/are pending in the application.
Of the above, claim(s) 42-47 & 51-54 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 27-29, 31-35, 37-41, & 48-50 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☑ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

Response to Amendment

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objections or rejections made in a previous Office Action that are not herein reinstated have been withdrawn.

4. Applicant has not complied with the requirements of 37 CFR 1.63(c), since the oath or declaration does not acknowledge the filing of any foreign application. A new oath or declaration is required in the body of which the present application should be identified by application number and filing date.

5. Applicant's election with traverse of Group I, claims 27-41 and 48-50 in Paper No. 10 is acknowledged. The traversal is on the ground(s) that the special technical feature of the instant invention is that it is a defective adenovirus encoding BDNF, and that Barde does not teach nor fairly suggest a defective recombinant adenovirus. This is not found persuasive because the specification defines "defective" adenovirus as simply adenovirus "deleted of certain viral regions" (page 4, line 3), which may be accomplished by substituting "the DNA sequence encoding BDNF" for viral sequences (sentence bridging pages 9-10). Barde discloses the substitution of

DNA that encodes BDNF in an adenovirus, in addition to such manipulations of DNA as promoter/enhancer elements and marker genes that would inherently entail the deletion of certain viral regions of the adenovirus, if only to make room for the splicing in of restriction sites by which the DNA encoding BDNF or other heterologous DNA could be inserted into the adenoviral genome.

The requirement is still deemed proper and is therefore made FINAL.

The restriction requirement has been made final. Applicant may seek to remove the finality of the restriction requirement only by petition at this point in the prosecution.

6. Claims 27-29, 31-34, 37-41, and 48-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a cDNA encoding BDNF (or a precursor protein) that is adequately characterized by chemical or structural characteristics, does not reasonably provide enablement for any substance or derivative that may be named "brain-derived neurotrophic factor" for reasons of record and the following. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The term "BDNF" carries no chemical or structural limitation to the recited chemical product, but only a functional limitation (neurotropism) and a source limitation (brain-derived). As such, the claims encompass any manner of substance that the brain produces that can be neurotrophic, such as neurotransmitters, adhesion molecules, even extracellular fluid (saline), etc. that are not envisioned by the instant specification. A protein's function cannot be adequately predicted from

its amino acid structure, so any "derivative" of BDNF produced by adding, deleting, or substituting amino acids would be unpredictable in regards to the desired properties of BDNF. It is suggested that the BDNF encoded by the adenovirus vector of the instant claims recite some chemical or structural limitations to keep the breadth of the claims commensurate with the disclosure.

Applicant's arguments filed 8/24/98 have been fully considered but they are not persuasive because Applicant has not amended the claims to recite some chemical or structural limitations to keep the breadth of the claims commensurate with the disclosure.

7. Claims 27-29, 31-35, 37-41, and 48-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barde in view of Le Gal La Salle. Barde discloses an adenovirus encoding human prepro/BDNF cDNA and transfected mammalian cells (column 18, line 32 to column 20, line 53, and column 38, line 7 to column 40, line 18). Barde did not teach specialized viral promoters for the nervous system or non-functional adenovirus E1 gene. Le Gal La Salle discloses replication deficient adenovirus vectors for gene transfer into neurons and glia that use RSV-LTR promoters and GFAP (page 988). Le Gal La Salle also had Michel Perricaudet as a co-author, who is also a co-inventor of the instant application. It is the Examiner's position that the replication deficient adenovirus of Le Gal La Salle had a non-functional E1 gene. The grounds of this rejection may be overcome by a 1.132 declaration by Michel Perricaudet that the Le Gal La Salle adenovirus had a functional E1 gene or other evidence (prior art) to the contrary. It would have been obvious to one of ordinary skill in the art at the time the invention was made

to use the BDNF of Barde and the adenovirus techniques of Le Gal La Salle in order to treat diseases of the nervous system amenable to BDNF treatment as suggested by Barde.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Applicant's arguments filed 8/24/98 have been fully considered but they are not persuasive because Barde has a prior filing date of 8/30/89. Applicant has not perfected the foreign filing date sought of 9/25/92, so the Le Gal La Salle reference is still held as prior art (2/12/93).

8. Claims 27-29, 31-35, 37-41, and 48-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barde in view of Wilson et al. (US 5,585,362). Barde discloses an adenovirus encoding human prepro/BDNF cDNA and transfected mammalian cells (column 18, line 32 to column 20, line 53, and column 38, line 7 to column 40, line 18). Barde did not teach specialized viral promoters for the nervous system or non-functional adenovirus E1 gene. Wilson teaches replication-defective adenovirus (abstract), RSV-LTR promoter, Ad 5 human adenovirus (column 11, lines 54-65) pfu/ml dosages (column 6, lines 25-55), and human cells from lung (column 8, lines 66-67). Wilson does not teach adenovirus comprising prepro/BDNF encoding cDNA. The effective date of Wilson is 9/11/92 (US Application No. 07/943,952). It would have been obvious to one of ordinary skill in the art at the time the invention was made to make and use the replication-defective adenovirus of Wilson with the cDNA sequences taught by Barde in

his replication defective retrovirus because Wilson discloses many advantages for the adenovirus vector for gene therapy, including its approval for clinical trials (column 2, lines 25-26), growth to extremely high titers for production purposes, usefulness in nondividing cells (column 2, lines 58-60), and other reasons (column 1, lines 54-62).

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (703) 308-6571. The examiner can normally be reached on Monday to Thursday from 0730 to 1800. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D., can be reached on (703) 308-3995. The fax phone number for this Group is currently (703) 308-4242, but Applicant should confirm this by phoning the Examiner before faxing.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Stephen Gucker

Stephen Gucker

February 9, 1999